

CLAIMS

What is claimed is:

1. An isolated nucleic acid molecule comprising a polynucleotide with a nucleotide
 5 sequence selected from the group consisting of:
 - (a) a nucleotide sequence encoding a heparanase II polypeptide comprising the
 amino acid sequence of SEQ ID NO:2
 - (b) a nucleotide sequence encoding a heparanase II polypeptide comprising the
 amino acid sequence at residues 42 through 534 of SEQ ID NO:2
 - 10 (c) a nucleotide sequence encoding a heparanase II polypeptide comprising the
 amino acid sequence at residues 42 through 129 of SEQ ID NO:2
 - (d) a nucleotide sequence encoding a heparanase II polypeptide comprising the
 amino acid sequence at residues 42 through 161 of SEQ ID NO:2
 - (e) a nucleotide sequence encoding a heparanase II polypeptide comprising the
 15 amino acid sequence at residues 130 through 534 of SEQ ID NO:2
 - (f) a nucleotide sequence encoding the heparanase II polypeptide comprising the
 amino acid sequence at residues 162 through 534 of SEQ ID NO:2 and
 - (g) a nucleotide sequence that is complementary to any of the nucleotide
 sequences of (a), (b), (c), (d), (e) or (f)
- 20 2. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide
 molecule of 1(a) comprises the nucleotide sequence at nucleotide positions 25
 through 1626 of SEQ ID NO:1, the polynucleotide molecule of 1(b) comprises the
 nucleotide sequence at nucleotide positions 148 through 1626 of SEQ ID NO: 1, the
 25 polynucleotide molecule of 1(c) comprises the nucleotide sequence at nucleotide
 positions 148 through 411 of SEQ ID NO:1, the polynucleotide molecule of 1(d)
 comprises the nucleotide sequence at nucleotide positions 148 through 507 of SEQ ID
 NO:1, ~~the polynucleotide molecule of 1(e) comprises the nucleotide sequence at~~
 nucleotide positions 412 through 1626 of SEQ ID NO:1 and the polynucleotide
 30 molecule of 1(f) comprises the nucleotide sequence at nucleotide positions 508
 through 1626 of SEQ ID NO:1

3. The isolated nucleic acid molecule of claim 1 wherein the polynucleotide molecule comprises a nucleotide sequence encoding a heparanase II polypeptide comprising the amino acid sequence of SEQ ID NO:2
- 5 4. The isolated nucleic acid molecule of claim 1 wherein the polynucleotide molecule comprises a nucleotide sequence encoding a heparanase II polypeptide comprising the amino acid sequence at residues 42 through 534 of SEQ ID NO:2
- 10 5. The isolated nucleic acid molecule of claim 1 wherein the polynucleotide molecule comprises a nucleotide sequence encoding a heparanase II polypeptide comprising the amino acid sequence at residues 42 through 129 of SEQ ID NO:2
- 15 6. The isolated nucleic acid molecule of claim 1 wherein the polynucleotide molecule comprises a nucleotide sequence encoding a heparanase II polypeptide comprising the amino acid sequence at residues 42 through 161 of SEQ ID NO:2
- 20 7. The isolated nucleic acid molecule of claim 1 wherein the polynucleotide molecule comprises a nucleotide sequence encoding a heparanase II polypeptide comprising the amino acid sequence at residues 130 through 534 of SEQ ID NO:2
8. The isolated nucleic acid molecule of claim 1 wherein the polynucleotide molecule comprises a nucleotide sequence encoding a heparanase II polypeptide comprising the amino acid sequence at residues 162 through 534 of SEQ ID NO:2
- 25 9. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide molecule comprises the nucleotide sequence at nucleotide positions 25 through 1626 of SEQ ID NO:1,
- 30 10. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide molecule comprises the nucleotide sequence at nucleotide positions 148 through 1626 of SEQ ID NO:1

11. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide molecule comprises the nucleotide sequence at nucleotide positions 148 through 411 of SEQ ID NO:1

5 12. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide molecule comprises the nucleotide sequence at nucleotide positions 148 through 507 of SEQ ID NO:1

10 13. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide molecule comprises the nucleotide sequence at nucleotide positions 412 through 1626 of SEQ ID NO:1

15 14. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide molecule comprises the nucleotide sequence at nucleotide positions 508 through 1626 of SEQ ID NO:1

15. A vector comprising a nucleic acid molecule described in claim 1.

20 16 The vector of claim 15, wherein said nucleic acid molecule is operably linked to a promoter for the expression of a human heparanase polypeptide.

17. A host cell comprising the vector of claim 15.

25 18. The host cell of claim 17, wherein said host is a eukaryotic host.

19. The host cell of claim 17, wherein said host cell is a baculovirus cell.

30 ~~20. A method of obtaining a human heparanase polypeptide comprising culturing~~
the host cell of claim 17 and isolating said human heparanase polypeptide.

21. A human heparanase polypeptide produced by the method of claim 20.

22. A composition comprising a polypeptide according to claim 21 in a pharmaceutically acceptable carrier.

23. An isolated human heparanase polypeptide comprising an amino acid
5 sequence selected from the group consisting of:

- (a) an amino acid sequence of a heparanase II polypeptide comprising the amino acid sequence of SEQ ID NO:2;
- (b) a heparanase II polypeptide comprising the amino acid sequence at residues 42 through 534 of SEQ ID NO:2;
- 10 (c) a heparanase II polypeptide comprising the amino acid sequence at residues 42 through 129 of SEQ ID NO:2;
- (d) a heparanase II polypeptide comprising the amino acid sequence at residues 42 through 161 of SEQ ID NO:2;
- (e) a heparanase II polypeptide comprising the amino acid
15 sequence at residues 130 through 534 of SEQ ID NO:2 and;
- (f) a heparanase II polypeptide comprising the amino acid sequence at residues 162 through 534 of SEQ ID NO:2.

24. The isolated heparanase II polypeptide of claim 23 wherein the polypeptide
20 molecule comprises the amino acid sequence of SEQ ID NO:2.

25. The isolated heparanase II polypeptide of claim 23 wherein the polypeptide molecule comprises the amino acid sequence at residues 42 through 534 of SEQ
ID NO:2.

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26. The isolated heparanase II polypeptide of claim 23 wherein the polypeptide molecule comprises the amino acid sequence at residues 42 through 129 of SEQ
ID NO:2.

30 27. The isolated heparanase II polypeptide of claim 23 wherein the polypeptide molecule comprises the amino acid sequence at residues 42 through 161 of SEQ
ID NO:2.

28. The isolated heparanase II polypeptide of claim 23 wherein the polypeptide molecule comprises the amino acid sequence at residues 130 through 534 of SEQ ID NO:2.

5 29. The isolated heparanase II polypeptide of claim 23 wherein the polypeptide molecule comprises the amino acid sequence at residues 162 through 534 of SEQ ID NO:2.

30 29. A heparanase II enzyme comprising

- 10 (a) an isolated heparanase II polypeptide comprising the amino acid sequence at residues 42 through 129 of SEQ ID NO: 2; and
(b) and isolated heparanase II polypeptide comprising the amino acid sequence at residues 130 through 534 of SEQ ID NO:2

15 30. A heparanase II enzyme comprising

- (a) an isolated human heparanase polypeptide comprising the amino acid sequence at residues 42 through 161 of SEQ ID NO: 2; and
(b) and isolated human heparanase polypeptide comprising the amino acid sequence at residues 162 through 534 of SEQ ID NO:2

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31. A heparanase II enzyme comprising

- (a) an isolated human heparanase polypeptide comprising the amino acid sequence at residues 42 through 129 of SEQ ID NO: 2; and
(b) and isolated human heparanase polypeptide comprising the amino acid sequence at
25 residues 162 through 534 of SEQ ID NO:2

32. A composition comprising a polypeptide according to claims 26 through 43 in a pharmaceutically acceptable carrier

30 33. A isolated heparanase II polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 2, or a fragment thereof comprising an epitope specific to said polypeptide.

34. An antibody specific for the heparanase II polypeptides of claims 26-43.
35. The antibody of claim 34 which is a monoclonal antibody.
36. A hybridoma that produces an antibody according to claim 35.
37. An antibody according to claim 35 that is a humanized antibody.
38. A cell-free composition comprising polyclonal antibodies, wherein at least one of said antibodies is an antibody according to claim 34.
39. A method for the identification of an agent that alters heparanase activity, said method comprising:
- (a) determining the activity of the isolated heparanase II polypeptide
 - (i) in the presence of a test agent; and
 - (ii) in the absence of said test agent; and
 - (b) comparing the heparanase activity determined in step (a)(i) to the heparanase activity determined in step (a)(ii);
- whereby a change in heparanase activity in sample (a)(i) has compared to sample (a)(ii) indicates that said agent alters the activity of said heparanase II polypeptide.
40. The method of claim 39, wherein said agent increases heparanase activity.
41. The method of claim 39, wherein said agent inhibits heparanase activity.
42. The method of claim 39, wherein the determination of heparanase activity is ~~made by measuring the amount of radiolabeled heparin/heparan sulfate that is digested~~ by said human heparanase enzyme.
43. A method for inhibiting the enzymatic activity of an heparanase II polypeptide comprising the step of contacting said enzyme with an antibody specific for said enzyme, under conditions wherein the antibody binds the enzyme.

45 44. A method for treating a disease state comprising the step of administering to a mammal in need of such treatment an amount of an antibody according to claim 34 sufficient to inhibit heparanase II enzymatic activity in the tissues of said mammal.

46 45. A method for treating a disease state comprising the step of administering to a mammal in need of such treatment an amount of an agent sufficient to alter heparanase II enzymatic activity in the tissues of said mammal

10